## DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Claim Status*

Applicants' response of March 6, 2008, to the non-final action dated December 13, 2007 has been entered. Claims 15 and 48-50 are pending in the application. Claim 15 has been amended. Claims 1-13, 16, 21, 23-31, 33, 34, 39 and 41-47 have been cancelled and claims 48-50 newly added. Claims 15 and 48-50 are under current examination.

### *New Claim Rejections - 35 USC § 112- New Matter*

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 15 and 48-50 are newly rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art (hereafter the Artisan), that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR §1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 15 recites: "an amino acid sequence having at least 80% homology to the amino acid sequence of SEQ ID NO: 1". The instant specification is devoid of any description for the limitation of "at least 80%". Applicants state that support for the amendment appears, at page 8, lines 1-27. While the specification discloses an amino acid sequence having "at least about 80% homology...to the amino acid sequence shown by SEQ ID NO: 1" (first paragraph, p. 8), such recitation is not equivalent to or commensurate in scope with "at least 80% homology".

Thus, at the time the application was filed, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of "an amino acid sequence having at least 80% homology to the amino acid sequence of SEQ ID NO: 1", as claimed.

MPEP 2163.06 notes: "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that

"Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

This is a new matter rejection.

***Response & New Claim Rejections - 35 USC § 112, Written Description***

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claim 15 stands rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The rejection set forth on pp. 3-7 of the office action dated December 13, 2007 is maintained for claim 15 in modified form, and further applied to newly added claims 48-50, for reasons of record. Applicants are directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112 ¶1 "Written Description" Requirement, Rev. 1, 2008; at http://www.uspto.gov/web/menu/written.pdf.

The instant claims broadly embrace a method of screening for a drug candidate compound or its salt that inhibits the expression of a gene encoding a protein comprising an amino acid sequence having at least 80% homology to SEQ ID NO: 1, or partial peptides of the protein, wherein said protein has a neurofibrillary degeneration promoting activity or a neural cell death promoting activity. As the variant proteins having at least 80% homology to SEQ ID NO: 1 and its partial peptides retain specific biological activities, the claims require for the variant sequence structures to retain function, necessitating structure/function relationships.

Applicants disagree with the rejection, stating that the Examiner admits the specification discloses the species of SEQ ID NOS: 1, 6, 8, 10, 12, 14, 16, 18 and 20, but requires the

disclosure of more species. Applicants additionally state that Applicants' amendment of claim 15 overcomes the rejection. Applicants' arguments have been fully considered, but are not found persuasive.

As an initial matter, it is noted that instant claim 15 continues to encompass variants of SEQ ID NO: 1 having at least 80% homology, or partial peptides having a neurofibrillary degeneration promoting activity or a neural cell death promoting activity. Thus, it is not clear how the amendment of the claim has overcome the basis of the rejection.

As previously indicated, the specification is silent on any structure/function relationship for SEQ ID NO: 1 and its numerous claimed variants having neurofibrillary degeneration promoting activity, a neuronal cell death promoting activity. It is further unclear what variations are encompassed SEQ ID NOS: 1, 6, 8, 10, 12, 14, 16, 18, 20, as the variations may include any amino acid changes or alterations at any position in SEQ ID NO: 1, as well as partial peptides of SEQ ID NO: 1, that retain an activity encompassing a neural cell death promoting activity. The instant specification is silent on the specific alterations that distinguish SEQ ID NOS: 6, 8, 10, 12, 14, 16, 18, 20 from SEQ ID NO: 1, as all appear to encompass amino acid sequences of the same size and highly similar sequence to that of SEQ ID NO: 1, and are therefore not representative of the numerous variants encompassed by the claim. Moreover, the numerous variant sequences, are not completely described in the prior art or the present specification and include sequences yet to be discovered. Therefore, the breadth of the claims as reading on numerous variant proteins that retain the required biological activities, in view of the level of knowledge or skill in the art at the time of the invention, and the limited information provided in the specification, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of numerous variants and partial peptides of SEQ ID NO: 1, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied.

Therefore the previous grounds of rejection is maintained for claim 15 and further applied to newly added claims 48-50, for reasons of record, and the preceding discussion.

***Response & New Claim Rejections - 35 USC § 112-Scope of Enablement***

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claim 15 stands rejected under 35 U.S.C.§112, first paragraph, because the specification is not enabling for the full scope of the invention. The rejection set forth on pp. 7-12 of the office action dated December 13, 2007 is maintained for claim 15 in modified form, and further applied to newly added claims 48-50, for reasons of record.

The specification, while being enabling for a method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising hybridizing an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA, does not reasonably provide an enablement for a method of screening a compound or its salt inhibiting the expression of a gene for a protein comprising an amino acid sequence having at least 80% homology to SEQ ID NO: 1, or a partial peptide of said protein having a neruofibrillary degeneration promoting activity or a neuronal cell death promoting activity, as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants disagree with the rejection, stating that the Office admits the specification is enabled for a method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising hybridizing an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA. Applicants additionally state that Applicants' amendment of claim 15 overcomes the rejection. Applicants' arguments have been fully considered, but are not found persuasive.

It is noted that Applicants' amendment of claim 15 fails to limit the claim to the enabled scope previously indicated, and reiterated above. Instant claim 15 continues to encompass variants of SEQ ID NO: 1 having at least 80% homology, or partial peptides having a

neurofibrillary degeneration promoting activity or a neural cell death promoting activity, and further encompasses the inhibition of gene expression by any type of drug candidate compound. Thus, it is not clear how the amendment of the claim has overcome the grounds of the rejection, as the claim clearly encompasses a broader scope than that originally presented, wherein the method was limited to using a polynucleotide.

As previously noted, the inhibition of gene expression includes inhibition of promoter function either directly, or indirectly by inhibition of transcription factors. The instant specification, while teaching the amino acid of human neuronal cell death inducible putative kinase (NIPK, SEQ ID NO: 1), and the base sequence of DNA encoding the same (SEQ ID NO: 2, p. 69), fails to provide any information regarding the promoter sequences of genomic structure of the human NIPK gene. The specification if further silent on the transcription machinery controlling the expression of human NIPK, and additionally silent on how the transcription of the gene may be inhibited by a candidate compound. Thus, a person of skill in the art would need to engage in further experimentation to discover and characterize the transcription machinery of the human NIPK gene and the sequences controlling promoter activity to design a compound screening method to discover inhibitors of the human NIPK transcription machinery. Such experimentation thus constituting an undue burden on the skilled artisan.

As a second issue, the specification is silent on any structure/function relationship for SEQ ID NO: 1 and its numerous claimed variants having neurofibrillary degeneration promoting activity, a neuronal cell death promoting activity. It is further unclear what variations are encompassed by SEQ ID NOS: 1, 6, 8, 10, 12, 14, 16, 18, and 20, that may include any amino acid changes or alterations at any position in SEQ ID NO: 1, as well as partial peptides of SEQ ID NO: 1, that retain an activity encompassing a neural cell death promoting activity and the like. The instant specification is silent on the specific alterations that distinguish SEQ ID NOS: 6, 8, 10, 12, 14, 16, 18, 20 from SEQ ID NO: 1, as all appear to encompass amino acid sequences of the same size and highly similar sequence to that of SEQ ID NO: 1, and are therefore not representative of the numerous variants encompassed by the claim. The prior art at the time of filing did not teach the large number of possible sequence variants of SEQ ID NO: 1 that retain biological activities substantially the same nature as that of human NIPK protein.

Applicants have failed to address the issues outlined above. Moreover, base claim 15 has been amended to recite the method steps of screening for a drug candidate compound, comprising comparing a cell culture comprising a polynucleotide encoding a partial peptide of NIPK protein with said cell culture further comprising a test compound. However, the comparison fails to set forth a basis for assessment of differences between the cell cultures. Thus a person of skill in the art would not be apprised of what parameters are encompassed by said comparing and how to assess inhibition of gene expression by simply comparing cell cultures.

Therefore the previous rejection is maintained for claim 15 and is applied to newly added claims 48-50, for reasons of record and the preceding discussion.

***Response & New Claim Rejections - 35 USC § 102***

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claim 15 stands rejected under 35 U.S.C. 102(e) as being anticipated by Meyers et al. (U.S. Patent Application Publication No.: 2002/0034780; filed: Mar. 6, 2001). The rejection set forth on pp. 12-13 of the office action dated December 13, 2007 is maintained for claim 15, and further applied to newly added claims 48-50, for reasons of record.

Applicants disagree with the rejection, stating that Myers et al. disclose a protein having 100% identity to SEQ ID NO: 1 and screening methods of identifying a compound that modulates the activity of the protein kinase and the expression of the kinase gene, but do not disclose screening for an agent for neurodegenerative disease or diabetes, thus failing to disclose all of the elements of claim 15. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it should be noted that the rejection of the claims over Myers et al. has been applied to the extent that the instant claim encompasses an enabled method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising hybridizing an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA. Meyers et al provide screening methods for identifying a compound that modulates the activity of the kinase

protein as well as identifying a compound that modulates the expression of the kinase gene [¶¶ 0022-0024], wherein the compound or agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the kinase mRNA or the kinase gene [¶ 0019]. The antisense nucleic acid molecules, are described as "molecules that are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule, or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire kinase coding strand, or to only a portion thereof, e.g., all or part of the protein coding region (or open reading frame)" [¶ 0180]. Further disclosing: "A ribozyme having specificity for a kinase-encoding nucleic acid can be designed based upon the nucleotide sequence of a kinase cDNA disclosed herein e.g., SEQ ID NOS: 1, 3, 4, 6, 7, 9" [¶ 0185].

Not withstanding Myers et al. teaching disorders involving the pancreas as including those of the exocrine pancreas such as diabetes mellitus ¶ [0138], and disorders involving the brain that include, but are not limited to, disorders involving neurons, and disorders involving glia, such as astrocytes, oligodendrocytes, ependymal cells, and microglia ¶ [0122]; Applicants should note that the limitation wherein the compound or its salt is a candidate for a prophylactic or therapeutic agent for neurodegenerative disease or diabetes is not afforded patentable weight, because a drug compound may be a candidate for any disease and will remain nothing more than a candidate until proven otherwise. Thus, the limitation of a compound being a candidate for a disease amounts to nothing more than an intended use for the compound. As stated in MPEP 2106, II. Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. An example of such language includes statements of intended use.

Therefore the previous rejection is maintained for claim 15 and is applied to newly added claims 48-50, for reasons of record and the foregoing commentary.

***Conclusion***

**Claims 15 and 48-50 are not allowed.**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and

would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fereydoun G. Sajjadi, Ph.D.

Examiner, Art Unit 1633

/Anne Marie S. Wehbe/
Primary Examiner, Art Unit 1633